

A M E N D M E N T S

Please amend the subject application as set forth below.

In the Title:

After "Method" delete "and Reagent".

In the Claims:

Cancel claims 83, 84, 86, and 87 without prejudice.

Amend claims 88 through 90 inclusive and 93 through 101 inclusive as set forth below.

Claims 88 through 90 inclusive, 93, 94, 96, 98, 100, and 101, line 1, for "any of claims 82, 83, 85, or 86" substitute -- either of claims 82 or 85 --.

Claims 95 and 97, line 1, for "either of claims 82 or 84" substitute -- claim 82 --.

Claim 99, line 1, for "either of claims 85 or 87" substitute -- claim 85 --.

Pursuant to 37 CFR 1.121, a complete listing of all the claims as amended of the subject application, which is a continued prosecution application (CPA) filed on 26 September 2002, is set out below; treating, for purposes of 37 CFR 1.121(c), the continued prosecution application (CPA) filed on 26 September 2002 and its immediate parent application which was filed on 26 February 1999 as a single application.

Claims 1 through 81 inclusive (cancelled).

82. (Previously Presented) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, at least one deoxynucleotide defining a labeled deoxynucleotide comprising a detectable label or an attachment moiety capable of binding a detectable label, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled deoxynucleotide is complementary to a specific nucleotide at the predetermined target position, a

detectable primer-extension product is formed of the detection primer extended to include an extension portion incorporating the labeled deoxynucleotide; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of a detectable label in association with a labeled deoxynucleotide incorporated in an extension portion of a primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

83. (Cancelled)

84. (Cancelled)

85. (Previously Presented) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be

detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, at least one chain-terminating nucleotide analogue defining a labeled chain-terminating nucleotide analogue comprising a detectable label or an attachment moiety capable of binding a detectable label, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled chain-terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined target position, a detectable primer-extension product is formed of the detection primer extended to include an extension portion terminated with the labeled chain-terminating nucleotide analogue; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of a detectable label in association with a labeled chain-terminating nucleotide analogue terminating an extension portion of a primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

86. (Cancelled)

87. (Cancelled)

88. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85, wherein the target nucleic acid is obtained or derived from the cells of a patient and the detection of the specific nucleotide indicates predisposition to a genetic disease in the patient.

89. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85, wherein the analyzable amount of target nucleic acid is obtained by performing an amplification reaction on a sample of nucleic acid.

90. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85 wherein the target nucleic acid comprises an attachment moiety.

91. (Previously Presented) A method according to claim 90 wherein the target nucleic acid is immobilized on a solid matrix during step (b).

92. (Previously Presented) A method according to claim 90 wherein the target nucleic acid is immobilized on a solid matrix during step (c).

93. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85 in which the primer-end complement nucleotide is located in the target nucleic acid at a position immediately adjacent to the predetermined target position.

94. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85 wherein the detection-primer nucleotide sequence is from 10 to 40 nucleotides in length.

95. (Currently Amended) A method according to ~~either of claims 82 or 84~~ claim 82 wherein the nucleoside triphosphates of paragraph (c) include at least two deoxynucleotides, at least one of which deoxynucleotide comprises a detectable label or an attachment moiety capable of binding a detectable label.

96. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85 wherein each deoxynucleotide of the nucleoside triphosphates of paragraph (c) is a deoxyribonucleoside triphosphate selected from the group consisting of dATP, dGTP, dCTP, dUTP, and dTTP.

97. (Currently Amended) A method according to ~~either of claims 82 or 84~~ claim 82 wherein each deoxynucleotide of the nucleoside triphosphates of paragraph (c) is a deoxyribonucleoside triphosphate selected from the group consisting of dATP, dGTP, dCTP, dUTP, and dTTP and in which the detectable label is a radioisotope.

98. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85 wherein each chain-terminating nucleotide analogue of the nucleoside triphosphates of paragraph (c) is a dideoxyribonucleotide selected from the group consisting of ddATP, ddGTP, ddCTP, and ddTTP.

99. (Currently Amended) A method according to ~~either of claims 85 or 87~~ claim 85 wherein each chain-terminating nucleotide analogue of the nucleoside triphosphates of paragraph (c) is a dideoxyribonucleotide selected from the group consisting of ddATP, ddGTP, ddCTP, and ddTTP and in which the detectable label is a fluorescent group.

100. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85, wherein the polymerization agent is a DNA polymerase.

101. (Currently Amended) A method according to ~~any of claims 82, 83, 85, or 86~~ either of claims 82 or 85, wherein the primer extension product is removed from the target nucleic acid prior to analysis.